BIOELECTRONICS

Wiring-up ion channels

Coating nanowires with lipid bilayers allows the use of biological ion channels as biosensors.

Friedrich C. Simmel

In his famous *Neuromancer* trilogy[1–3], science-fiction author William Gibson equips his main characters with biochip implants that allow them to connect their brains to computer networks and 'upload' new knowledge or capabilities as needed. For instance, a hero of the story instantly becomes a jet pilot by simply loading the corresponding software into his brain.

An interface between biological cells and transistors — in the extreme case between a human brain and a computer — has been the dream not only of science-fiction authors, but also of scientists for many years now. Information transfer between the biological and the electronic realms would not only be important for futuristic applications such as the one mentioned above, but also for prosthetics and biosensing in general.

However, there is a significant problem with this: our brain works with ions, whereas computers use electrons to process information, and it is far from straightforward to marry these two worlds. Communication requires 'translation' of ions to electrons through electrochemical processes or capacitive coupling of ionic and electronic signals. Reporting in the *Proceedings of the National Academy of Sciences*, Nipun Misra and co-workers[4] now show how this coupling might be achieved using lipid-coated silicon nanowires.

Misra *et al.* covered an electrically contacted nanowire with a lipid bilayer — a biomembrane resembling the one that surrounds biological cells — and inserted protein pores into these membranes (Fig. 1). Cell membranes are densely packed with specialized proteins that are responsible for interaction and signal exchange with the cell's environment. Some of these membrane proteins contain tiny channels through which water and ions can flow — often in a highly specific manner. These so-called ion channels can switch between a conducting and a non-conducting state depending on the binding of small molecules or the voltage across the membrane, a property called 'gating'. For this reason, ion channels have been previously referred to as "life's transistors"[5].

Misra and colleagues were able to incorporate two model ion channels into the lipid bilayer surrounding their nanowires — the well-studied peptide pores gramicidin A and alamethicin — and use them to detect pH changes in the solution. Without the bilayer, the solution pH directly affects the protonation state of the nanowires' silicon dioxide surface, which in turn influences their conductance — similar to traditional ion-sensitive field-effect transistors. The dense lipid bilayer, however, makes the nanowires unresponsive to pH. The pH sensitivity is regained only when protons can flow through the ion channels inserted into the bilayer. Importantly, Misra *et al.* showed that this effect can be 'gated'. The gramicidin A pore can be blocked by calcium ions, and the researchers could verify that the pH response of the nanowires was indeed rendered calcium-sensitive by the ion channels. Alamethicin, on the other hand, is known to be a voltage-gated pore. When a bias was applied to the nanowire with respect to an electrode in solution, the pH sensitivity was shown to be voltage-dependent as expected.

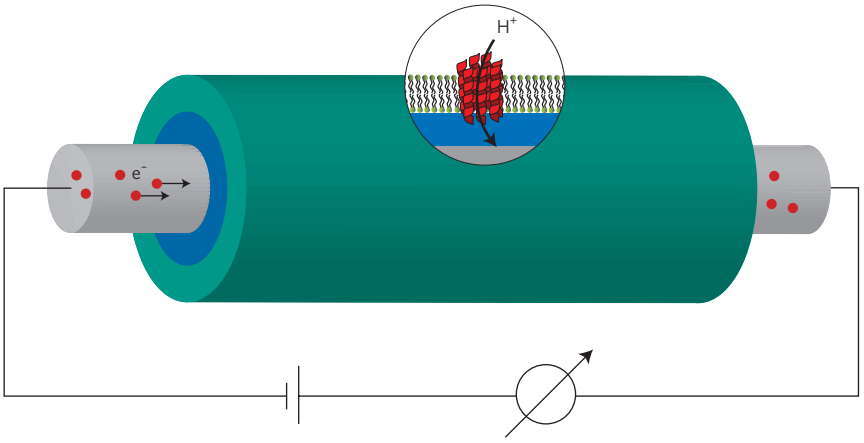

Figure 1 | Schematic of a silicon nanowire coated with a lipid bilayer (coloured green) containing ion-conductive peptide pores (shown in red). Protons (H^+) flowing through the ion channels change the pH of the water film (blue layer) between the lipids and the nanowire. This chemically modifies the surface of the nanowire and thereby change its conductance. Current through the nanowire is carried by electrons (e^-). This effect can therefore be used to effectively transduce ionic to electronic signals.

As noted above, there have already been many attempts to couple whole cells or reconstituted ion channels in membranes to electronics. In fact, in a series of seminal papers, Peter Fromherz and his group were able to demonstrate bidirectional information transfer between neurons and transistors[6,7]. Here, the coupling between the weak neural signals and the transistors proved to be notoriously difficult, mainly because the large salt-solution-filled 'cleft' between cells and chip prevented their direct interaction by electrical polarization. Recent advances towards cell-based biosensors were made using genetically modified cells overexpressing a serotonin neuroreceptor channel[8]. The first use of reconstituted — that is, cell-free — ion channels as biosensors had already been shown in 1997 by Cornell *et al.*[9], but this did not result in a large burst of research activity at that time.

Today, many researchers believe that chemically synthesized nanowires could revolutionize the field. Their small dimensions perpendicular to the direction of electrical transport make their conductance exceedingly sensitive to the nanowires' surface, and therefore chemically modified nanowires seem to be ideally suited as components for biosensors[10,11].

In the case of the work reported by Misra *et al.*, an extra advantage is the dense and smooth coverage of the lipid bilayer over the nanowires, resulting in an only 4-nm-thick water-filled gap between membrane and wire. Owing to the high

effective ion concentration close to the surface, this crucially helps to transduce the ion channel's sensitivity to the nanowire.

This step having been made, a number of formidable challenges remain to make the ion-channel-based biointerface a reality. In their experiment, Misra and co-workers used two simple peptide pores, which are commonly used as 'test devices'. It will be quite challenging to incorporate 'real' ion channels with more versatile functions into the lipid membrane coating the nanowires. This would truly result in new ion-channel-based biosensors that combine the extraordinary biochemical and electronic sensitivities of their components. For neuroprosthetics, however, it will also be important to make information transfer bidirectional, that is, to controllably transfer electronic to ionic or chemical signals. Furthermore, at present it is unclear how such devices would be made to function *in vivo*. ❐

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TOPOLOGICAL PHASES

Wormholes in quantum matter

Proliferation of so-called anyonic defects in a topological phase of quantum matter leads to a critical state that can be visualized as a 'quantum foam', with topology-changing fluctuations on all length scales.

Kareljan Schoutens

There is no end to the list of remarkable quantum phases of matter that can emerge if simple building blocks are endowed with just the right interactions and are cooled to low enough temperatures. In many cases, the essence of such phases can be captured by an order parameter. Think of a quantum ferromagnet, for example, with the order parameter specifying the direction of the magnetization. More intricate quantum phases, which can arise in frustrated quantum magnets (which possess disordered ground states) or in systems of strongly correlated electrons or cold atoms, lack such telling diagnostics, and it becomes something of an art to characterize the quantum order that they hide. Charlotte Gils and colleagues, writing on page 834 of this issue[1], show how particular quantum phases can be visualized as a quantum foam — a surface with topology-changing quantum fluctuations on all length scales.

The logic that leads Gils *et al.* to their remarkable physical picture is best followed in two steps. First they consider so-called topological phases of matter in two-dimensional (2D) systems, following a microscopic description originally given by Michael Levin and Xiao-Gang Wen[2]. These topological phases are seemingly featureless quantum liquids, lacking any form of local order. But their special nature manifests itself at the edge of a system, where gapless edge modes arise, or, for systems defined on a surface with non-trivial topology, in characteristic ground-state degeneracies. The topological order also affects the quantum statistical properties of defects. Avoiding the restrictions for three-dimensional systems, where bosonic or fermionic statistics are the rule, defects over 2D topological phases tend to be anyons. Interchanging anyons can lead not only to prefactors of ±1, as for bosons and fermions, respectively, but to 'any' phase or even to matrices acting on an internal quantum space. For the 'Fibonacci anyons' (which feature in the paper of Gils *et al.*[1]) the dimensionality of the *n*-particle internal space is precisely the *n*th element of the Fibonacci sequence (1, 1, 2, 3, 5, 8, …).

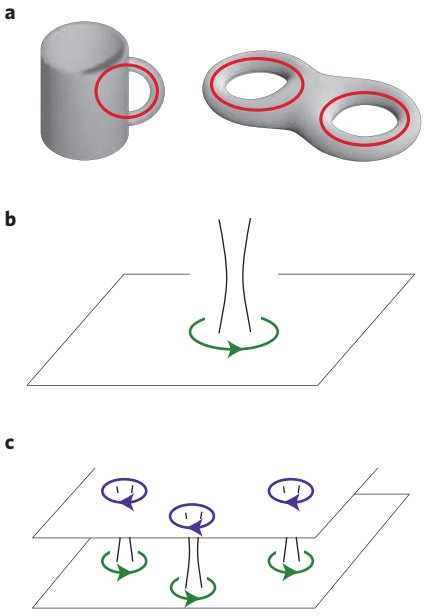

Figure 1 | Topology matters. **a**, For the topology of a 2D surface, all that counts is the number of incontractible loops. **b**, A defect in a chiral 2D topological quantum liquid can be pictured as a tiny current circulating in an incontractible loop around a hole, creating a 'chimney'. **c**, When there are two sheets connected by such chimneys, proliferation of these wormholes drives a topological phase to a critical point, visualized as a quantum foam.

Topological phases are known to occur in fractional quantum Hall systems, where electrons are confined to a 2D Flatland, exposed to a strong perpendicular magnetic field (of many Teslas) and cooled to low temperatures (in the millikelvin range). The magnetic field breaks the time-reversal symmetry, causing the characteristic edge modes to be chiral — that is, having a preferred direction and therefore one-way traffic along the edges. But the topological phases of Levin and Wen[2] are time-reversal invariant. It is then natural to visualize these states as anyonic quantum liquids living on a double sheet, with each sheet corresponding to a specific chirality of edge modes.

In the second step of their analysis, Gils *et al.*[1] add a term to the Levin–Wen Hamiltonian, which lowers the energy of specific defects. The defects can be visualized as 'wormholes' connecting the two sheets (Fig. 1). Driving the strength of the extra term to a critical value leads to